January 18, 2005

F.J. Sonny Maher
Panel Manager
American Chemistry Council
Fatty Nitrogen Derivatives Panel
Nitriles Task Group
1300 Wilson Boulevard
Arlington, VA 22209

Dear Mr. Maher:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Ether Nitriles Category posted on the ChemRTK HPV Challenge Program Web site on February 23, 2004. I commend American Chemistry Council Fatty Nitrogen Derivatives Panel Nitriles Task Group for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that the Task Group advise the Agency, within 90 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Donald Rodier, Acting Chief of the HPV Chemicals Branch, at 202-564-7633. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Ether Nitriles Category

Summary of EPA Comments

The sponsor, the Fatty Nitrogen Derivatives Panel Nitriles Task Group of the American Chemistry Council, submitted a test plan and robust summaries to EPA for the fatty nitrogen derived (FND) ether nitriles category dated December 29, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on February 24, 2004. The category consists of three sponsored substances: 3-(isodecyloxy)propanenitrile (CAS No. 64354-92-3); 3-(tridecyloxy)propanenitrile (CAS No. 68239-19-0); and 3-(C8-10-alkoxy)propanenitriles (CAS No. 68784-39-4). The submitter included seven non-sponsored substances (members of the fatty nitrogen derived (FND) nitriles category, also reviewed by EPA) to provide supporting data for the category members.

EPA has reviewed this submission and has reached the following conclusions:

1. Category Justification. The grouping of the three ether nitriles into one category is supported by structural similarities. However, additional information is needed to support the rationale for the use of supporting substances. The lack of experimental data for the sponsored substances and the absence of a rationale in the test plan for using supporting substance data are significant sources of uncertainty. The submitter needs to provide experimental data for category members or, in the case of health and ecological effects, provide an adequate basis for using data on the proposed supporting chemicals.

2. Physicochemical Properties. The submitter needs to provide data for melting point, vapor pressure, and water solubility.

3. Environmental Fate. EPA agrees with the submitter that there are sufficient data for category members for photodegradation, stability in water and fugacity for the purposes of the HPV Challenge Program. Data are needed for biodegradation.

4. Health Effects. Without information demonstrating that data from the supporting FND alkyl nitriles are applicable to the ether nitriles, EPA does not consider the data provided adequate to characterize any health effects endpoints for this category. Furthermore, the submitted information is inadequate to support classification of these chemicals as closed system intermediates (CSIs) eligible for reduced testing in the HPV Challenge Program. Unless additional information is provided to support the CSI claim, the submitter needs to address repeated-dose and reproductive toxicity for the category.

5. Ecological Effects. Without data linking the supporting FND alkyl nitriles to the ether nitriles, EPA does not consider the data provided adequate to predict the aquatic toxicity of the ether nitrile category members. The submitter needs to provide a basis for extrapolating supporting data to the FND ether nitriles or provide experimental data for representative category members.

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.

EPA Comments on the Ether Nitriles Category Challenge Submission

Category Definition

The Fatty Nitrogen Derived (FND) Ether Nitriles category includes three chemicals containing 3-alkyloxy derivatives of propanenitrile. These substances are 3-(isodecyloxy)propanenitrile (CAS No. 64354-92-3), 3-(tridecyloxy)propanenitrile (CAS No. 68239-19-0), and 3-(C8-C10-alkyloxy) derivatives of propanenitrile (CAS No. 68784-39-4). The alkyloxy portions of these ether nitriles are composed of saturated linear or branched aliphatic hydrocarbons that vary in carbon number from C8 to C13.

The submitter included seven non-sponsored substances (members of the fatty nitrogen derived (FND) nitriles category) to provide supporting data for the category members. These substances are dodecanenitrile (CAS No. 2437-25-4), octadecanenitrile (CAS No. 638-65-3), 9-octadecenenitrile (CAS No. 112-91-4), coco nitriles (CAS No. 61789-53-5), hydrogenated tallow nitriles (CAS No. 61790-29-2), tallow nitriles (CAS No. 61790-28-1), and soya nitriles (CAS No. 68514-67-0). These non-members are long chain alkyl nitriles; none contain an ether function at the 3-position and four have olefinic alkyl groups.

Category Justification and Use of Supporting Chemical Data

The submitter's rationale for grouping the three fatty nitrogen derived (FND) ether nitriles into one category is based on structural similarities that result in surfactant-like properties that in turn are expected to have physicochemical properties, environmental fate and toxicities similar to an even larger family of surfactants, including the FND alkyl nitriles. Seven of these FND alkyl nitriles are included in the test plan as supporting chemicals based on their structural similarity to the sponsored substances.

For the three sponsored chemicals, the submitter states that the differences between the carbon numbers C8 to C13 in the alkyl portion of the 3-alkyloxypropanenitriles do not impart measurable differences in biodegradation, aquatic toxicity, or toxicity to mammalian systems. The submitter supports the inclusion of fatty nitrogen derived (FND) alkyl nitriles as supporting substances by stating that these substances have HPV endpoint values that are similar to those of the FND ether nitriles (although no experimental data were submitted for the ether nitriles). Among the supporting FND alkyl nitriles, the submitter notes that over the carbon number range of these supporting chemicals (C8-C18), there are no significant differences in physicochemical properties. In addition, the submitter notes that the three supporting mixture substances that are derived from natural oils (e.g., coco, tallow and soya), have toxicological properties similar to those of the two single chemical FND alkyl nitriles. Overall, the submitter concludes that "there are no significant differences among the chemicals in the category that reasonably can be expected to result in differences in the HPV/Screening Information Sets (SIDS) endpoints."

Although the grouping of the FND ether nitriles into one category is supported by structural similarities, the submitter provided no experimental data for the three category members. All associations between supporting substances and category members are derived from comparisons of estimated values for the FND ether nitriles to experimental and estimated values for the FND alkyl nitriles. This lack of experimental data for the sponsored chemicals, and the absence of an adequate rationale in the test plan for extrapolating FND alkyl nitriles data to the FND ether nitriles, are significant sources of uncertainty. Therefore, EPA believes that the test plan as proposed is not adequately supported. The submitter needs to provide an adequate basis for using data on FND alkyl nitriles to characterize the FND ether nitriles category members or provide experimental data for category members.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The data supplied by the submitter for FND alkyl nitriles cannot be used to support the FND ether nitriles category because the ether group in these chemicals results in the ether nitriles having different polarities and geometries than the alkyl nitriles. These differences may result in physicochemical properties that are different from the supporting alkyl nitrile chemicals.

The submitted data for boiling point and partition coefficient are adequate for the purposes of the HPV Challenge Program. Estimated boiling points above 300 °C and estimated Log P values for these chemicals are adequate for the HPV Challenge Program.

Melting point. The submitted melting point data are not adequate for the purposes of the HPV Challenge Program. The submitter provided estimated values, using EPIWIN, of 48 °C for 3-(isodecyloxy)-propanenitrile, and 86 °C for 3-(tridecyloxy)propanenitrile. According to OECD guidelines, melting points

above 0 °C need to be measured. The submitter needs to provide measured data for these chemicals.

Vapor pressure. The submitted vapor pressure data are not adequate for the purposes of the HPV Challenge Program. The submitter provided estimated values, using EPIWIN, of 0.0012 mm Hg (0.15 Pa) for 3-(isodecyloxy)propanenitrile, and 0.00004 mm Hg (0.0053 Pa) for 3-(tridecyloxy)- propanenitrile. According to OECD guidelines, vapor pressure values above $1x10^{-5}$ Pa need to be measured. The submitter needs to provide measured data for these chemicals.

Water solubility. The submitted water solubility data are not adequate for the purposes of the HPV Challenge Program. The submitter provided estimated values, using EPIWIN, of 9.2 mg/L for 3-(isodecyloxy)propanenitrile and 0.26 mg/L for 3-(tridecyloxy)propanenitrile. According to OECD guidelines, solubility values above 1 µg/L need to be measured. The submitter needs to provide measured data for these chemicals.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The data provided by the submitter for photodegradation, stability in water and fugacity are adequate for the purposes of the HPV Challenge Program.

Biodegradation. The submitter did not provide biodegradation data for any of the FND ether nitrile category members, and proposed the use of analog data to fulfill this endpoint. Robust summary data were provided only for supporting alkyl nitriles, none of which contain an ether functionality. The submitted data are not adequate for the purposes of the HPV Challenge Program. The comparison of the alkyl nitriles to the ether nitriles may not be appropriate. The ether group in these chemicals may result in biodegradation properties that are different than those of the alkyl nitriles. The submitter needs to provide measured biodegradation data, following OECD TG 301, for 3-(isodecyloxy)propanenitrile (branched) and 3-(tridecyloxy)propanenitrile (straight-chain).

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

The submitter did not provide health effects data for the ether nitriles category members. The submitter provided only acute toxicity data for four of the supporting FND alkyl nitriles and genetic toxicity (gene mutations) data for two of the supporting FND alkyl nitriles, and cited a plan to conduct testing of one FND nitrile for genetic, reproductive and developmental toxicities. It is not known, however, what effect the presence of the ether function in the ether nitriles category members may have on the toxicities of these substances in relationship to the FND alkyl nitriles. Therefore, without information demonstrating that existing and planned toxicity data from the supporting FND alkyl nitriles are applicable to the ether nitriles, EPA does not consider the data provided adequate to characterize the ether nitriles category

The submitter claims that the ether nitriles are closed system intermediates (CSIs) eligible for reduced health effects testing in the HPV Challenge Program. The Guidance for Testing Closed System Intermediates for the Challenge Program http://www.epa.gov/chemrtk/guidocs.htm allows for a reduced testing protocol provided certain criteria are met. The information required to support a CSI claim must address the following:

I. Site information
    A. Number of sites.
    B. Basis for “closed process” conclusion at each site.
        1) Process description.
        2) Monitoring data showing no detection.
        3) In the absence of monitoring data, the basis for believing that releases do not occur.
    C. Data on “presence in distributed products.”
II. Information on transport (mode, volume, controls, etc)
III. A data search showing that the chemical is not present in other end products.

EPA believes that the submitted information is inadequate to satisfy the requirements for classification of the ether nitriles as CSIs eligible for reduced testing in the HPV Challenge Program for the following reasons.

IB and IC. *Basis for closed process conclusion at each site. Process description. Monitoring data showing no detection. In the absence of monitoring data, the basis for believing that releases do not occur. Data on "presence in distributed products."*

According to the test plan, reaction vessels used to produce FND ether nitriles category chemicals are part of multi-purpose, closed system operations. The process description is not sufficiently detailed to provide a reasonable basis to conclude that the process is closed.

The test plan indicates that monitoring data are not routinely collected to assess for potential exposures to FND ether nitriles category chemicals. The absence of monitoring data leaves no basis for believing that these chemicals are not released during manufacture, processing, and consumption and that exposure to the chemicals does not occur. The test plan also states that wastewater generated during periodic equipment cleaning is treated on-site or incinerated, but information on the concentrations of the subject chemicals in wastewater discharges is not provided.

II. *If transport occurs, information on the mode of transport, volume, type of consignment, and controls during transport and transfer at dispatching and receiving sites*:

Transfer descriptions lacked details. The submitter needs to address handling practices at all sites.

III. *Supporting evidence that the chemical is not present in other end-products*.

While the information provided is reasonable, analytical data would help substantiate that the chemical is not present in other end-products. Odor threshold data would also be supportive.

Unless additional information is provided to support the "closed system intermediate" claim, the submitter needs to address all health effects endpoints for the purposes of the HPV Challenge Program.

Ecological Effects (fish, invertebrates, and algae)

EPA disagrees with the submitter that available data are adequate. The ether nitriles and supporting FND alkyl nitriles show a pattern of estimated ecotoxicities based on chain length and degree of branching, but no experimental data are available for the ether nitriles. Although the measured LC_{50} and EC_{50} data for the supporting substances provided in the test plan are generally within one order of magnitude, there are no data linking the supporting substances with the category members. Without this information, no conclusion can be made as to how well the supporting substances predict the aquatic toxicity of the ether nitrile category members. Consequently, EPA does not consider the data provided adequate to characterize the ether nitriles category. The submitter needs to provide a basis for using data on FND alkyl nitriles for the FND ether nitriles category members, or provide experimental data for category members.

Specific Comments on the Robust Summaries

None.

Followup Activity

EPA requests that the submitter advise the Agency within 90 days of any modifications to its submission.